

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 7/06	A1	(11) International Publication Number: WO 99/49839 (43) International Publication Date: 7 October 1999 (07.10.99)
(21) International Application Number: PCT/KR98/00234 (22) International Filing Date: 31 July 1998 (31.07.98) (30) Priority Data: 1998/11521 1 April 1998 (01.04.98) KR (71)(72) Applicant and Inventor: PARK, Hyo, Suk [KR/KR]; 978-18, Banbae-dong, Seocho-ku, Seoul 137-060 (KR). (74) Agent: HUH, Sang, Hoon; Hyecheon Building, 13th floor, 831, Yeoksam-dong, Kangnam-ku, Seoul 135-792 (KR).		(81) Designated States: CA, CN, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>
(54) Title: TOPICAL LIQUID COMPOSITION FOR PROMOTING HAIR GROWTH AND PROCESS OF MANUFACTURING THEREOF (57) Abstract The invention herein relates to a topical liquid composition for promoting hair growth, comprising natural ingredients with no side-effects, which is effective in promoting hair growth and preventing hair loss. More particularly, the invention relates to the topical liquid composition for promoting hair growth, comprising the extracts which are formed by immersing the mixture of powders of Pinelliae Rhizoma, Caryophylli Flos, Rubi Fructus, Zanthoxyli Fructus, Vitis Fructus, Salviae Radix, and Thujae Semen in oil and ethanol, respectively, followed by aging for a fixed period of time.		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

TOPICAL LIQUID COMPOSITION FOR PROMOTING HAIR GROWTH AND PROCESS OF MANUFACTURING THEREOF

BACKGROUND OF THE INVENTION

5 Field of the Invention

The invention herein relates to a topical liquid composition for promoting hair growth, comprising natural ingredients with no side-effects, which is effective in promoting hair growth and preventing hair loss. More particularly, the invention relates to the topical liquid composition for promoting hair growth, comprising the
10 extracts which are formed by immersing the mixture of powders of Pinelliae Rhizoma, Caryophylli Flos, Rubi Fructus, Zanthoxyli Fructus, Viticis Fructus, Salviae Radix, and Thujae Semen in oil and ethanol, respectively, followed by aging for a fixed period of time.

15 Description of the Prior Art

Hair has a life span of a sort as hair continuously falls out, and new hairs begin to grow. In general, alopecia denotes a loss or absence of hair and typically includes alopecia areata. It is physiological in a normal sense that a person should shed 70 to 80 hairs a day. Alopecia also includes the balding from excessive hair loss and
20 thinning, in whole or in part. In the case of severe alopecia, a patient should consult a dermatologist since it may be a systemic disease.

As for the forms of alopecia, they could be congenital due to hereditary cause or acquired symptoms from various environmental factors. As for the direct causes, they include excessive stress, tension on the scalp muscle, excessive secretion of male
25 hormone, androgen, or relative reduction in secretion of female hormone, seborrheic dermatitis and atopic constitution, and physical stimulation. In particular, excessive intake of fat and exposure to pollution have been recognized as major causes of alopecia.

Presently, several methods have been disclosed for the prevention and

treatment of aforementioned alopecia. For example, Korean Unexamined Patent No. 91-106 discloses a method of using a rhododendron extract as active ingredient. Korean Unexamined Patent No. 96-40346 discloses a hair-growth promoter using a pine biloba extract: the Korean Unexamined Patent No. 90-64 relates to a hair-growth promoter using a quartz porphyry. Korean Unexamined Patent No. 90-2757 discloses a hair-growth promoter using a silkworm.

Nevertheless, there is a great need for further improving the shortcomings of the conventional methods since they do not provide expected therapeutic effectiveness in promoting hair growth and preventing hair loss.

10

SUMMARY OF THE INVENTION

The objective of the invention herein is to provide a topical liquid composition for promoting hair growth, comprising of natural ingredients with no side-effects, which is effective in promoting hair growth and preventing hair loss, by means of immersing various natural ingredients in oil and ethanol, respectively, followed by aging for a fixed period of time.

15

Detailed Description of the Invention

This invention relates to a topical liquid composition for promoting hair growth comprising extracts of Pinelliae Rhizoma, Caryophylli Flos, Rubi Fructus, Zanthoxyli Fructus, Viticis Fructus, Salviae Radix, and Thujae Semen.

20

In addition, the invention relates to a process of preparing the topical liquid composition for promoting hair growth, wherein 20 - 40 weigh parts of a mixture of respective powders of Pinelliae Rhizoma, Caryophylli Flos, Rubi Fructus, Zanthoxyli Fructus, Viticis Fructus, Salviae Radix, and Thujae Semen is immersed in 100 weight parts of oil, and 100 weight parts of ethanol. Then, the oil and ethanol extracts, so obtained via aging for 5 - 10 days, are blended in the respective weight ratio of 1 : 10 -

25

The invention is explained in more detail as set forth hereunder. The invention relates to a topical liquid composition for promoting hair growth, comprising a mixture of extracts of *Pinelliae Rhizoma*, *Caryophylli Flos*, *Rubi Fructus*, *Zanthoxyli Fructus*, *Vitidis Fructus*, *Salviae Radix*, and *Thujae Semen*, obtained by means of immersing said ingredients in oil and ethanol, respectively.

The characteristics of each active ingredient according to the manufacturing process are provided in more detail as set forth hereunder. According to this invention, *Pinelliae Rhizoma*, *Caryophylli Flos*, *Rubi Fructus*, *Zanthoxyli Fructus*, *Vitidis Fructus*, *Salviae Radix*, and *Thujae Semen* is prepared in the form of powder.

The detailed description of each active ingredient are as follows:

Pinelliae Rhizoma is a tuber after removing the cork layer of *Pinellia ternata* Breitenbach (Araceae), which is distributed throughout Korea. There are various preparations of *Pinelliae Rhizoma*. For example, the fresh *Pinelliae Rhizoma* is gathered in the summer and dried in the sun. The blue *Pinelliae Rhizoma* is prepared with boiled rice, and the Kang-*Pinelliae Rhizoma* is prepared with ginger and boiled rice. The Pup-*Pinelliae Rhizoma* is packaged by adding boiled rice, lime, licorice, and ginger. The *Pinelliae Rhizoma* pottage is a malt prepared by adding wheat flour, red bean, and apricot stone to the Kang-*Pinelliae Rhizoma* in a powder. As for the indications, *Pinelliae Rhizoma* has the effect of drying dampness, resolving phlegm and preventing vomiting. An appropriate amount of 3 - 10g/day of softy milled crude drug has been clinically used by topical means.

Caryophylli Flos is the bud of the *Caryophylli Flos* plant (*Eugenia caryophyllata* Thumb, Myrtaceae), which is customarily called Kong Ding Xiang in China. *Caryophylli Flos* is mainly cultivated in Tanzania, Malaysia, Indonesia, and Guandong in China. When the green bud of *Caryophylli Flos* changes into red during the period from September to next March, it is carefully plucked. With the removal of a flower stalk, it is dried in the sun prior to use. *Caryophylli Flos* is effective for clearing away heat and toxic material, and warming the kidney. It is administered in a dose

of 1 - 3g.

Rubi Fructus is an unripe fruit of *Rubus Coreanus* Miq. (Rosaceae). The unripe fruits are picked during the summer, placed in boiling water and dried in the sun prior to use. Rubi Fructus is known to be effective for tonifying the kidney and decreasing
5 urination. It is administered by decoction in a dose of 3 - 10g.

Zanthoxyli Fructus is the skin of the ripe fruit of *Zanthoxylum Piperitum* D.C. or other members of the Rubaceae family, with the removal of the seeds. The ripe fruits are picked in autumn, dried in the sun or extracted prior to use. Zanthoxyli Fructus is effective for relieving pain, killing parasites, inhibiting cough, and soothing asthma. It
10 is topically administered in an appropriate amount of 3 - 6g.

Vitidis Fructus is a fruit of *Vitex Rotundifolia* L. Fil. (Verbenaceae). In general, it is picked during the summer, dried in shade and parched until turning yellow. Vitidis Fructus is effective for clearing and dissipating heat, clearing the head, and brightening the eyes. It is preferable that this crude medicine be administered in a dose
15 of 5 - 10g per day.

Salviae Radix is mainly produced in several regions of China, such as Anhui, Jiangsu, and Sichuan. Its therapeutic effects include invigorating blood, removing stagnation, cooling blood, reducing carbuncles, clearing heat in the heart, and soothing irritability. Salvia Radix usually is administered in a dose of 5 - 15g by decocting.

20 Lastly, Thujae Semen is the seed of *Thuja Orientalis* Linne (Cupressaceae). Its ripe seed is collected in the early winter. The testae of the seed is removed, and the core is dried in the sun. Thujae Semen is distributed throughout Korea and China. In particular, the main areas of production include Chechon, Choongbuk of Korea, and Shandong, Heilong, Heilong of China. Thujae Semen is good for nourishment and
25 pacifying the liver. It is generally administered in a dose of 10 - 20g.

The invention herein is characterized in that seven different herbal components are prepared in a powder form by a bead mill in the range of 80 - 100 mesh. Then, 20 - 40 weight parts of the mixed powder is immersed in 100 weight parts of oil and 100

weight parts of ethanol for 5 - 10 days. The reason for limiting the total contents of the herbal components to 20 - 40 weight part to 100 weight parts of oil and 100 weight parts of ethanol lies in the fact that if such contents are less than 20 weight parts, the herbal extraction capacity is reduced. If it exceeds 40 weight parts for immersion, the improvement of therapeutic effect cannot be expected, and the manufacturing process is not deemed to be economical. Further, it is preferable that the blending ratios of each herbal component be in the range of 1:10 to the total extract. It is also preferable that the blending ratio be equal in weight ratio per each herbal component. It is preferable that one or more vegetable oils be blended, which are selected from the group consisting of sesame oil, perilla oil and Thujae Semen oil, and prepared by the commonly used method. In particular, it is most preferable that the blending ratio be 50% of sesame oil, 20% of perilla oil, and 30% of Thujae Semen oil by weight.

The topical solution according to this invention is prepared with the blending ratio of 1:10 - 15 between the oil extract and ethanol extract having the active ingredients. In the case of the oil extract, Caryophylli Flos and Zanthoxyli Fructus having volatile characteristics are extracted. In the case of the ethanol extract, Pinellia Rhizoma, Rubi Fructus, Viticis Fructus, Salviae Radix and Thujae Semen are extracted. The topical solution, derived from the mixture of these herbal extracts, is effective in promoting hair growth and preventing hair loss without any side-effects.

The above preparation is topically used in a liquid form, and its use is very convenient. It is preferable that the composition be applied in a dose of 1,000 - 3,000 mg per day. It is most preferable that the topical preparation be applied to the affected epidermal site for 1 - 2 times daily in a dose of 1 - 3cc.

The following examples illustrates various aspects of this invention but are not to be construed to limit the claims in any manner whatsoever.

Example

First, Pinelliae Rhizoma, Caryophylli Flos, Rubi Fructus, Zanthoxyli Fructus,

Vitidis Fructus, Salviae Radix and Thujae Semen, respectively, were made into powder by means of meshing machine. The powders were evenly mixed in equal proportions by weight in a stirring machine.

30g of a herbal powder mixture was immersed into 100cc of vegetable oil consisting of 50% of sesame oil, 20% of perilla oil, and 30% of Thujae Semen oil by weight for 7 days. Separately, in the same procedure as described above, 30g of the herbal powder mixture was immersed into 100cc of ethanol for 7 days. Then, a mixture consisting of 5% of oil extract, 55% of ethanol extract, and 40% of purified water by weight was well blended in a stirring machine to yield a topical liquid preparation.

Experimental example 1: Application of a topical liquid preparation to the areas of hair loss induced by drugs and/or radiological treatment

With the sample of 10 patients, the topical liquid preparations, so prepared from the example, were applied to the areas of hair loss induced by drug administration and/or radiological exposure in dose of 3cc for two times per day for the duration of 6 months. As a result, the topical liquid preparation was shown to have remarkable hair-growth effect including generation of new hair roots in 8 patients.

Comparative experimental example 1: Application of a topical liquid preparation to the areas of hair loss induced by drugs and/or radiological treatment

The currently available drugs for hair growth are directed to the improvement of blood circulation in the surrounding area of scalp in the hair root. These include the Minoxidil agent which was approved in 1979 by the Food and Drug Administration of U.S.A. as a hair-growth agent, i.e., Baldmin® (Choong-wae Pharmaceutical Co., Ltd.), Moxidil® (Hanmi Pharmaceutical Co., Ltd.), Minoxidil® (Hyundai Pharmaceutical Co., Ltd.), Doctor Mo® (Pacific Pharmaceutical Co., Ltd.), and Grobix® (Kyungin Pharmaceutical Co. Ltd.). With the same testing condition as above, however, these

preparations failed to exhibit the therapeutic effects in 10 patients with hair loss induced by the drug administration and/or radiological exposure.

Experiment example 2: Application of a topical liquid preparation to the areas of hair loss induced by atopic dermatitis

In general, an atopic patient is vulnerable to atopic alopecia as well as atopic dermatitis. Under the same conditions as described in the example 1, the topical liquid preparation, so prepared from the example, was applied to the areas of hair loss induced by atopic dermatitis. As a result, the topical liquid preparation was effective in the treatment of atopic dermatitis and implanting new hair roots.

Comparative experimental example 2 : Application of a topical liquid preparation to the areas of hair loss induced by atopic dermatitis

Under the same conditions as the experimental example 1, the hair-growth agents of the comparative experimental example 1 were applied to the areas of hair loss induced by atopic dermatitis. However, there were no therapeutic effects with respect to the treatment of atopic dermatitis.

Experimental example 3: Application of a topical liquid preparation to the areas of hair loss induced by alopecia areata

Under the same conditions as described in the experimental example 1, the topical liquid preparation, so prepared from the example was applied to the areas of hair loss induced by alopecia areata. As a result, the preparation exhibited a remarkable therapeutic effect observable even with the naked eyes.

Comparative experimental example 3 : Application of a topical liquid preparation to the areas of hair loss induced by alopecia areata

Under the same conditions as the experimental example 1, the hair growth

agents of the comparative experimental example 1 were applied to the areas of hair loss induced by alopecia areata. However, the agents failed to exhibit any therapeutic effects on alopecia areata by gross observation.

5 **Experimental example 4 : Skin toxicity test**

Since the topical liquid preparation of this invention for promoting hair growth comprises herbal medicine, such as Pinelliae Rhizoma, Caryophylli Flos, Rubi Fructus, Zanthoxyli Fructus, Viticis Fructus, Salviae Radix and Thujae Semen, no adverse reaction or toxicity was observed.

10 The above test results showed that when the topical liquid preparation according to this invention was applied to the areas of hair loss, the hair loss therein was significantly reduced 15 days after the administration. The topical liquid preparation was proven to be quite effective against the hair loss induced by adverse reaction to drug administration and/or radiological treatment. When the topical liquid preparation
15 was applied to atopic patients, it was effective in the treatment of atopic dermatitis while preventing atopic hair loss. In addition, the preparation was shown to be very effective in the treatment of hair loss induced by alopecia areata.

Since the topical liquid preparation of the invention herein contains herbal medicine as active ingredients, the preparation does not have any side-effects or adverse
20 reaction from the use thereof.

CLAIMS**What is claimed is:**

1. A topical liquid composition for promoting hair growth, comprising the extracts of Pinelliae Rhizoma, Caryophylli Flos, Rubi Fructus, Zanthoxyli Fructus, Viticis Fructus, Salviae Radix, and Thujae Semen, as active ingredients.
5
2. A topical liquid composition for promoting hair growth according to claim 1, wherein each of said active ingredients comprises in an equal weight ratio.
- 10 3. A topical liquid composition for promoting hair growth according to claim 1 or 2, wherein the oil extract and ethanol extract containing said active ingredients are mixed in the ratio of 1 : 10 - 15% by weight.
4. A topical liquid composition for promoting hair growth according to claim 3,
15 wherein one or more oil components of said oil extract is selected from the group consisting of sesame oil, perilla oil, and Thujae Semen oil.
5. A process of manufacturing the topical liquid composition for promoting hair growth, wherein 20 - 40 weight parts of the powder comprising Pinelliae Rhizoma, Caryophylli Flos, Rubi Fructus, Zanthoxyli Fructus, Viticis Fructus, Salviae Radix
20 and Thujae Semen are immersed in 100 weight parts of oil and 100 weight parts of ethanol, respectively, and aged for 5 - 10 days, after which are mixed in the weight ratio of 1 : 10 - 15.
- 25 6. A process of manufacturing the topical liquid composition for promoting hair growth according to claim 5, wherein each of said active ingredients comprises in an equal weight ratio.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR 98/00234

A. CLASSIFICATION OF SUBJECT MATTER

IPC⁶: A 61 K 7/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC⁶: A 61 K 7/06

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Patent Abstracts of Japan, Vol.14, No.211(C-715), 1990, JP 2-48517 A (SHISEIDO CO.).	1-6
A	Patent Abstracts of Japan, Vol.14, No.211(C-715), 1990, JP 2-48514 A (SHISEIDO CO.).	1-6
A	Patent Abstracts of Japan, Vol.17, No.211(C-1052), 1993, JP 4-352710 A (FUJII K.K.).	1-6
A	Database WPI on Epoque, week 8943, London: Derwent Publications Ltd., AN 89-314088, Class B04, JP 12-33207 A (CHUWA INT.), abstract.	1-6
A	Database WPI on Epoque, week 8537, London: Derwent Publications Ltd., AN 85-226622, Class B04, JP 60-146829 A (ROHTO), abstract.	1-6
A	FR 2 558 727 A1 (R. RAHMATHOLLAH) 02 August 1985 (02.08.85), totality.	1-6
A	WO 97/16 158 A1 (Y. SHIN) 09 May 1997 (09.05.97).	1-6

☐

Further documents are listed in the continuation of Box C.

☒

See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

23 November 1998 (23.11.98)

Date of mailing of the international search report

16 December 1998 (16.12.98)

Name and mailing address of the ISA/
Austrian Patent Office
Kohlmarkt 8-10; A-1014 Vienna
Facsimile No. 1/53424/535

Authorized officer

Irmeler

Telephone No. 1/53424/133

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR 98/00234

Im Recherchenbericht angeführtes Patentdokument Patent document cited in search report Document de brevet cité dans le rapport de recherche	Datum der Veröffentlichung Publication date Date de publication	Mitglied(er) der Patentfamilie Patent family member(s) Membre(s) de la famille de brevets	Datum der Veröffentlichung Publication date Date de publication
FR A1 2558727	02-08-85	keine - none - rien	
WO A1 9716158	09-05-97	keine - none - rien	